

SYNTHETIC BIOLOGY

REPLICATING MILK PROTEINS IN GENETICALLY MODIFIED MICROBES BY USING GENETIC SEQUENCES FROM MANY MAMMALS COULD GIVE US ANIMAL-FREE DAIRY

A better whey

S RAMADORAI, RAMAN SRINIVASAN
& S SHIVARAMAKRISHNA

Ramadorai is former vice-chairman, TCS, Srinivasan is head, TCS Ignite, and Shivaramakrishna is researcher, TCS

IN THE LAST two articles ([bit.ly/2YJWthe](#) and [bit.ly/3iX1FWt](#)), we saw the vital role played by heme-containing molecules in ferrying oxygen. Furthermore, heme lends red meats their characteristic colour, flavour and aroma. Interestingly, the plant kingdom has a heme-analog as well, called leg-hemoglobin, found in the roots of legumes. Scientists are decoding the molecular mechanisms of nature. Entrepreneurs are applying these mechanisms to produce valuable molecules like leghemoglobin in a scalable and sustainable manner. Synthetic biology has paved the way for startups producing hitherto impossible materials ranging from flexible digital displays to brontosaurus burgers! We begin this story with another valuable protein, the iron-binding lactoferrin, found in small quantities in milk.

Lactoferrin, a lesser-known whey protein, has many important functions. Discovered only in 1960, it plays a key function in binding and transporting iron, which in turn, is essential for ferrying oxygen through blood. Scientists now understand that lactoferrin modulates, in multiple ways, immunity in new-born babies. For instance, it promotes a beneficial gut microbiome among infants.

Mammals, by definition, make milk. Mammalian biology has evolved a variety of milks perfected for particular evolutionary niches. Even the egg-laying, web-footed, teal-less, duck-billed platypus secretes milk, a valuable milk, rich in a rare protein with potent antibacterial properties. Australian scientists have found that this novel protein has a unique three-dimensional folding that opens an entirely new class of antibiotics.

Closer home, the Vechur cow (now almost extinct), a dwarf cow, native to the Kuttanad region of Kerala, yields milk con-

taining as much lactoferrin as human breast milk. This is said to be one reason for its well-known medicinal properties.

Affluent consumers in China are spurring a seemingly endless upsurge in demand for lactoferrin-enriched infant formula. The presence of lactoferrin in human breast milk lets babies absorb more than 50% of iron available in breast milk, as opposed to only 12% absorption of iron from infant formula. Historically, practitioners of Ayurveda have prepared medicines with Vechur cow milk for health management in infants and convalescents.

Kerala is also home to a long tradition of theoretically informed empirical study of elephant biology and behaviour. Several texts including the "Ayurveda of Elephants" exist as living texts. Scientific research on elephant lactation reveals the broad similarities in mammalian milk composition, but also reveals the marvelous ability of nature to dynamically alter the composition of milk as the requirements of a growing child change. Especially amongst elephants, as the calf gets bigger, its energy needs increase significantly. Hence, the composition of the milk

changes to include more fats and proteins. Like the cow and humans, elephants also secrete immunity boosting proteins like lactoferrin in their milk.

Milk, a superfood, plays a critical role in our nutrition. India is the world's largest producer of milk, and has over 100 million dairy farmers. However, super cows are not needed to make this superfood. Happy cows are a good start. Animal management practices and environmental conditions influence milk composition. There is a business logic to "five-star" dairy facilities, where cows are free. They are even pampered with piped-in music and cow-controlled back-scratching robots and showers! Individual cows even actively choose when to exercise, and when to be milked, all at their own convenience. Thus, the actual composition of cow's milk can vary with the individual animal, its breed, stage of lactation, age and health status.

Compared to, say, ground beef, let alone a rib-eye steak, milk is a much simpler munificence of nature. It is mostly water. On an average, 87% of cow's milk is water. Lactose, a simple sugar consisting of glucose and galactose sub-units, makes

up 4.4%. Milk fats average to about 4.5% and minerals constitute less than 1%. Milk proteins make up 3.8%.

Milk proteins, in turn, consist of almost 80% caseins, and about 20% whey proteins. Caseins are further subdivided into alpha, beta, gamma, and kappa-caseins. The caseins are found in conjunction with fat as globular structures called 'micelles', held in a colloidal suspension in water. However, caseins do precipitate under acidic conditions. Thus, when the milk turns sour due to acid-producing bacteria, or if one adds a little bit of lemon juice, it curdles and the caseins precipitate.

Whey proteins, on the other hand, are water soluble. They can be further fractionated into alpha-lactalbumin, beta-lactoglobulin, serum albumin, and immunoglobulins. Lactoferrin and a few other proteins are also present in minute quantities. Ryan Pandya and Perumal Gandhi, the co-founders of Perfect Day foods, obtained a US patent in March 2018 that grants them the intellectual property rights to reconstruct animal-free dairy products, including milk. They do this by replicating milk proteins using genetically modified microbes by using genetic sequences from: "cow, human, sheep, goat, buffalo, camel, horse, donkey, lemur, panda, guinea pig, squirrel, bear, macaque, gorilla, chimpanzee, mountain goat, monkey, ape, cat, dog, wallaby, rat, mouse, elephant, opossum, rabbit, whale, baboons, gibbons, orangutan, mandrill, pig, wolf, fox, lion, tiger, echidna, or woolly mammoth."

In the future, a fussy child could demand a woolly mammoth milkshake. In the next article, we will look at how such wonders might be made, and the potential for disruption that such a technology might have for our 100 million marginal dairy farmers.

The co-founders of Perfect Day foods, obtained a US patent in March 2018 that grants them the IPR to reconstruct animal-free dairy products, including milk